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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/442,542	11/18/1999	LONNIE D SHEA	4100.002000	6026

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/442,542	SHEA ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-18,48,54-65,106-108 and 118-130* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,17,18,48,54-66,106-108 and 118-130* is/are rejected.

7)☒ Claim(s) *15 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/15/04 has been acknowledged.

Claims 14-18, 48, 54-65, 106-108, 118-130 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The finality of the rejection of the last Office action is withdrawn in view of new grounds of rejection below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims *14-18, 48, 54-65, 106-108 and 118-130 are* rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 1-53 of U.S. Pat. No. 6,642,363 in view of claims 1-35 of U.S. Pat. No. 6797738, claims 1-36 of U.S. Pat No. 6281256, claims 1-77 of US 5763416 and claims 1-130 of U.S. Pat. No. 594296.

The claims of pending U.S. App. No. 09442542 are drawn to a composition comprising a porous modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interaction (i.e. RGD) and a nucleic acid segment in non-covalent association with the matrix.

The claims of USPN 6,642,363 are drawn to a modified alginate matrix comprising at least one alginate chain section, which is covalently bonded to at least one cell attachment polypeptide or RGD-polypeptide, which promotes cell adhesion and growth. However the '363 does not claim a modified alginate matrix, which is in the form of porous matrix and contains nucleic acid molecules.

The claims of USPN 6797738 and 6281256 are drawn to a porous polymer alginate material, wherein the pores are formed by gas foaming (CO_2) and leaching out the particulate material (NaCl). The claims are further drawn to the polymer material comprising a drug and/or viable cells contained within the pores of porous polymer.

The claims of USPN 5763416 and 5942496 are drawn to a composition comprising one or more nucleic acid segments in association with structural bone-compatible matrix. The claims are further drawn to a matrix composition that contains one or more genes selected from parathyroid hormone (PTH: PTH1-34) gene, a bone morphogenetic protein gene (BMP: BMP-2A, BMP-2B, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7 or BMP-8 gene), a growth factor gene, a growth factor receptor gene, a cytokine gene or a chemotactic factor gene, transforming growth factor (TGF) gene, a fibroblast growth factor (FGF) gene, a granulocyte/macrophage colony stimulating factor (GMCSF) gene, an epidermal growth factor (EGF) gene, a platelet derived growth factor (PDGF) gene, an insulin-like growth factor (IGF) gene, a latent TGF-.beta. binding protein (LTBP) gene or a leukemia inhibitory factor (LIF) gene.

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the RGD-linked alginate matrix of USPN 6,642,363 by introducing a pore structure in view of USPN 6797738 and 6281256 using gas foaming and/or particulate

leaching. One would have been motivated to introduce porous structure in the matrix to contain drugs or viable cells in order to make a drug delivery system. It would have been further obvious to one ordinary skill in the art to substitute a drug with a nucleic acid molecule in view of USPN 5763416 and 5942496 which teaches a method of transferring nucleic acid segments into viable cells of an animal by contacting a matrix structure containing one or more nucleic acid of interest. One would have been motivated to do so to genetically modify the cells in order to produce recombinant proteins of interest. One would have a reasonable expectation in doing so, since modification of alginate chains to include a molecule of interest and making a porous structure by gas foaming and particulate leaching was routine in the art at the time the instant invention was made. In addition one would have a reasonable expectation of success in making and using a porous alginate matrix containing nucleic acid because such a composition had been well within the reach of one ordinary skilled in the art at the time the instant invention was made. Thus the invention as claimed is an obvious variation over cited patents of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14, 17, 18, 48, 106-108 and 118-130 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al (Biomaterials 18:583-590, 1997) in view of

Fang et al (PNAS 03:5773-5758, 1996) and Kawada et al (FEBS Letts. 408;43-46, 1997).

The scope of instant claim encompasses a porous alginate matrix that comprises a molecule bound to alginate chain that mediates cellular interaction and a nucleic acid segment in a non-covalent association with the porous alginate matrix.

Shapiro teaches a porous alginate sponges for the cell culture and transplantation. The cited art teaches the making of cross-link alginate sponges that contains porous structures (page 584, col.1, para.3-4). The cited art further teaches investigation by electron microscopy reveled that the pore size can be controlled by variation in alginate and cross-linker concentration (page 586, table-2, fig-3). The cited art further teaches tissue cell culture in alginate sponges (page 585, col.1 para. 2). Even though the cited art teaches a porous alginate matrix the cited art does not teach incorporation of nucleic acid molecules in the matrix and that the matrix is capable of mediating cellular interaction via alginate chain section.

Fang teaches gene-activated matrices (GAMs) comprising a biodegradable matrix containing nucleic acid molecules. The cited art teaches the preparation of collagen sponges that contains plasmid DNA molecules (page 5753 abstract, page 5754, col.2). Regarding claims 125, 106-108 the cited art teaches the transplantation of gene-activated matrices in an animal model that resulted in the expression of a marker gene, PTH-34, BMP-4 or TGF-b genes in host animals (page 5755, fig-2, page 5756, fig-4, page 5757, fig-5). The cited art further teaches that implantation of porous matrices (sponges) containing the nucleic acid molecules results in the genetic modification of host cells that in turn produces the gene product of interest (page 5756 fig-4; page 5757 col.2 para.2). Regarding claims 118-121 the cited art teaches that the nucleic acid incorporated in the matrix encompasses plasmid expression vectors encoding PTH-34, BMP-4 genes, which stimulates bone progenitor cells. Regarding claims 122-124 the cited art teaches that nucleic acid of interest encompasses marker genes, PTH-34, BMP-4 and TGF-b genes that are capable of modulating fibroblast growth and immune response. Regarding claims 126-130 the cited art teaches that plurality of nucleic acid segments can be introduced in gene-activated matrices which

transfeccts host cells at the site of transplantation. For example the cited art teaches transfer and expression of plasmid mixture (BMP-4 + PTH1-34) in host animals using gene-activated matrices (page 5756, col.2 para.2).

Kawada teaches alginate contains mixture of oligosaccharides that are capable of mediating cellular interaction (see abstract). The cited art further teaches isolation of alginate oligosaccharide having proliferative activity (page 45 col.1). For example the cited art teaches that alginate oligosaccharides showing proliferative effects have gulonic acid in the reduced terminus (page 45 col.2, fig-4). Regarding claim 14 specifically the cited art teaches that alginate derived oligosaccharides included –4)-O-a-D-mannopyranuronic acid residues (page 45 col.1 para 3).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of Shapiro who teaches a porous alginate sponges by incorporating nucleic acid molecules as taught by Fang. One would have been motivated to do so to induce gene expression of interest in host cells at the site of sponge transplantation. One would have a reasonable expectation of success in doing so, since genetic modification of host cells by transplanting a porous matrix has been routine in the art at time the instant invention was made. In addition given the scope of a molecule that mediates a cellular interaction the alginate matrix inherently contains alginate chains section bonded to various oligosaccharides that mediates cellular interaction (see Kawada). Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If

attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER
1/05/07